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10/577,119	04/13/2007	Gary Kevin Robinson	05794.00004	1176

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EXAMINER	
PORTNER, VIRGINIA ALLEN	
ART UNIT	**PAPER NUMBER**
1645	

NOTIFICATION DATE	DELIVERY MODE
08/09/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/577,119	ROBINSON ET AL.	
	Examiner	Art Unit	
	GINNY PORTNER	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 May 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2 and 4-20* is/are pending in the application.

4a) Of the above claim(s) *13-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2 and 4-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/2010*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-2, 4-20 are pending; claims 13-20 are withdrawn from consideration; claims 1-2, 4-12 are under consideration.

Objections/Rejections Withdrawn

1. ***Specification*** The disclosure objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01. The hyperlinks located in paragraphs [012], and [031] were removed.
2. ***Specification*** The disclosure objected to because of the following informalities: at [0023], line 4, appears as the word "Burkhoderia" and should be ---Burkholderia-----; the spelling typo has been corrected.
3. ***Claim Objections*** Claims 1-12 objected to because of the following informalities, specifically for reciting non-elected inventions has been obviated by Applicant's amendment limiting the examined claims to down regulation of LuxR with a peptide hydrolase.
4. Withdrawn, Claims 1-12 are rejected under 35 U.S.C. 102(b) as being anticipated by Berka (US PG-Pub 2003/0027310, published February 6, 2003) in light of the amendment of independent claim 1 to require the peptide hydrolase to irreversibly hydrolyzing an amide bond in peptide or protein; the hydrolase of Berka et al cleaving homoserine lactone.

Information Disclosure Statement

5. The information disclosure statement filed May 20, has been considered, For those reference presented in English

6. The EP foreign patent submitted in German on May 20, 2010 fails to comply with 37 CFR 1.98(a)(3) because it does not include a concise explanation of the relevance, as it is presently understood by the individual designated in 37 CFR 1.56(c) most knowledgeable about the content of the information, of each patent listed that is not in the English language. It has been placed in the application file, but the information referred to therein has not been considered.

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Objections/Rejections Maintained

Response to Arguments

7. Applicant's arguments filed May 20, 2010 have been fully considered but they are not persuasive.

8. Maintained, The objection to claim 4 for reciting a plurality of non-peptide hydrolyases, specifically chemical compounds, such as CNBr, is traversed on the grounds that the instant Specification has been amended to define peptide hydrolyases to encompass compounds.

9. It is the position of the examiner that peptide hydrolyases are not compounds, such as CNBr. CNBr is a compound that will hydrolyze an amide bond. Claims 1 and 4 should recite compounds for the hydrolysis of a peptide bond or amide bonds, rather than referring to all of the compounds as peptide hydrolyases (enzymes).

Maintained, Claim Rejections - 35 USC § 112

10. Maintained.Claim 4 recites the limitation "BNPS skatole," "CNBr", "formic acid", iodosobenzoic acid" and NTCB"" in dependence upon claim 1 which recites "peptide hydrolase" is traversed on the grounds that the instant Specification has been amended to define peptide hydrolyases to encompass compounds.

11. It is the position of the examiner that peptide hydrolyases are enzymes. Where applicant acts as his or her own lexicographer to specifically define a term of a claim contrary to its ordinary meaning, the written description must clearly redefine the claim term and set forth the uncommon definition so as to put one reasonably skilled in the art on notice that the applicant intended to so redefine that claim term. *Process Control Corp. v. HydReclaim Corp.*, 190 F.3d

1350, 1357, 52 USPQ2d 1029, 1033 (Fed. Cir. 1999). The term "peptide hydrolase" in claims 1 and 4 is used by the claim to mean "compounds that hydrolyze amide bonds", while the accepted meaning is "enzymatic cleavage of peptide/amide bonds by proteins with enzymatic activity." The term is indefinite because the specification does not clearly redefine the term.

New Amendments/New Claim Limitations/New Grounds of Objection/Rejection
Specification

1. The amendment filed May 20, 2010 is objected for minor informalities:

2. Original paragraph [0027] defined "Peptide hydrolyases to be enzymes", but this has been changed to now include the term "compound", referring to the compounds : BNPS Skatole, CNBr, formic acid, iodosobenzoic acid, NTCB (2-nitro-5-thiocyanobenzoic acid), set forth in claim 4, the amendment of the Specification being shown immediately below:

Please amend paragraph [0027] of the application as published (US 20070264715) as follows:

[0027] Peptide hydrolases are enzymes or compounds that inreversibly hydrolyse amide bonds in peptides and proteins. Peptide hydrolases are widely distributed and are involved in many different biological processes, from activation of proteins and peptides to degradation of proteins.

3. While original claim 4 recited these terms in association with the claim limitations "peptide hydrolyases", the BNPS Skatole, CNBr, formic acid, iodosobenzoic acid, NTCB (2-nitro-5-thiocyanobenzoic acid) compounds are not peptides, nor are they enzyme hydrolyases.

4. Hydrolyases are classified as **EC 3** in the EC number classification of enzymes.

Hydrolyases can be further classified into several subclasses, based upon the bonds they act upon:

- EC 3.1: ester bonds (esterases: nucleases, phosphodiesterases, lipase, phosphatase)
- EC 3.2: sugars (DNA glycosylases, glycoside hydrolase)
- EC 3.3: ether bonds
- EC 3.4: peptide bonds (Proteases/peptidases)
- EC 3.5: carbon-nitrogen bonds, other than peptide bonds
- EC 3.6 acid anhydrides (acid anhydride hydrolyases, including helicases and GTPase)
- EC 3.7 carbon-carbon bonds
- EC 3.8 halide bonds
- EC 3.9: phosphorus-nitrogen bonds
- EC 3.10: sulfur-nitrogen bonds
- EC 3.11: carbon-phosphorus bonds
- EC 3.12: sulfur-sulfur bonds
- EC 3.13: carbon-sulfur bonds

Therefore the amendment to the instant Specification at paragraph [0027] introduces a lack of clarity into the Specification, and introduces a meaning for the phrase "peptide hydrolase" that is repugnant to the meaning of the phrase in the art.

Claim Objections

5. Claim 1 is objected to because of the following informalities: Claim 1 recites the phrase "modulating the ability of LuxR" which includes increasing or decreasing LuxR activity, but the claim has been amended to be directed to only down regulating LuxR; the claim is internally inconsistent. Appropriate correction is required.

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Please Note: The following prior art rejections are being made of record in light of Applicant's claims amendments to require the peptide hydrolase to be capable of irreversibly hydrolyze a peptide or protein bond.

1. Claims 1, 4, 5 (cell death), 6(Pseudomonas), 7(glass test tubes), 9, 11-12 are rejected under 35 U.S.C. 102(b) as being anticipated by Slaton (1958). Salton disclose the instantly claimed invention directed to a method that comprises the step of :

2. treating the bacterial with a peptide hydrolase capable of irreversibly hydrolyzing amide bonds in peptide and proteins, wherein the peptide hydrolase is trypsin(see title, page 514, Table 1, page 515), in a dispensable liquid (was dispensed into test tubes, page 515) together with an aqueous carrier, specifically phosphate buffer pH 7.6. While Slaton does not discuss LuxR and quorum sensing in the bacteria, Slaton carried out the same or equivalent methods step of

treating bacteria with trypsin which resulted in irreversible peptide and protein bond hydrolysis resulting in cell death (page 515, paragraph 2, Table 1, Pseudomonas) and inhibition of biofilm formation on the glass test tubes surfaces. . Inherently Slaton anticipates the instantly claimed invention as now claimed. Inherently the reference anticipates the now claimed invention. Atlas Powder Co. V IRECA, 51 USPQ2d 1943, (FED Cir. 1999) states Artisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art...However, the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior arts functioning, does not render the old composition patentably new to the discoverer. AThe Court further held that Athis same reasoning holds true when it is not a property but an ingredient which is inherently contained in the prior art≅.

13. Claims 1,2,5,6,7,9, 11 and 12 are rejected under 35 U.S.C. 102(b) as being anticipated by Zhang et al WO2003/068951 or 102(e) PG-Pub 2005/0155088 (citations taken from PG-Pub for ease of pointing out citations).

14. Zhang et al disclose the instantly claimed invention directed to a method,

Instant claim 1: the method comprising the step of down regulating quorum sensing [0033,0043] by treating the bacteria with a peptide hydrolase capable of irreversibly hydrolyzing amide bonds in peptides [0029, pages 3-4, “cleaves the amide linkage", an amide linkage being a peptide bond].

Instant claim 2, 6: wherein the homologue of LuxR is any one of traR(see Ex. 2[0077], page 8; EcbR [0049], ExpR[0065 and [0034]; CepR1[0062], [0006 “Vibrio species"… Agrobacterium

tumefaciens, Burkhholderia cepacia, Erwinia carotovora, Erw.chrysanthemi, Erw. Stewartii, Pseudomonas aeruginosa, P. aureofaciens, Serratia liquifaciens, [0004 "gram negative bacteria"].

Instant claim 5: to inhibit biofilm formation [0007].

Instant claim 7: wherein the surface is plastic [0076 "Eppendorf tubes or 96-well plates- 0077].

Instant claim 9, 11-12: administering to the bacteria a composition comprising a peptide hydrolase and an aqueous carrier [0077 "sterilized reaction mixture" (which is a dispensable liquid) pH 7, colorant-dye "5-bromo-4-chlor-3-indolyl B-D-galactopyranoside" "blue colonies", claims 11, 14, 16].

Zhang et al anticipates the instantly claimed invention as now claimed.

Claim Rejections - 35 USC § 103

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

16. Claims 8 (catheter), 9 (non-aqueous) , 10 (biocide), 12 (spray) are rejected under 35 U.S.C. 103(a) as being unpatentable over Zhang et al as applied to claims 1-3, 5-7, 9, 11-12 above, and further in view of Berka et al .

a. See discussion of Zhang et al above. Zhang et al teach methods of down regulating LuxR quorum sensing by treating a bacteria with a peptide hydrolase (acylase, amide bond cleavage) for disrupting, preventing or reducing the ability of the bacteria to infect plant and animal tissues or to form biofilms [0007], but differs from the instantly

claimed invention by failing to show the composition to comprise a detergent/biocide, in spray form, with a non-aqueous carrier, to a catheter surface.

b. Berka teach compositions that contains a detergent/biocide, teach spray form compositions, non-aqueous carrier, to a catheter surface in analogous art for the purpose of preventing biofilm formation by down regulating quorum sensing .

(Berka claim 34) A method for preventing biofilm development on a liquid-solid interface by one or more microorganisms, comprising administering an effective amount of a composition comprising one or more polypeptides having lactonohydrolase activity and a carrier to the liquid-solid interface to degrade one or more lactones produced by the one or more microorganisms, wherein the one or more lactones are involved in the formation of the biofilm. As well as… surfaces of medical devises, catheters, orthopedic devices, implants, industrial water processing systems which include materials that are plastic, and metal. [0172] Thus, the biofilm is a complex assembly of living microorganisms embedded in an organic structure composed of one or more matrix polymers which are secreted by the resident microorganisms.

[0173] Biofilms can develop into macroscopic structures several millimeters or centimeters in thickness and cover large surface areas. These formations can play a role in restricting or entirely blocking flow in plumbing systems, decreasing **heat transfer in heat exchangers**, or causing pathogenic problems in municipal water supplies, food processing, **medical devices (e.g., catheters, orthopedic devices, implants)** and often decrease the life of **materials** through corrosive action mediated by the embedded microorganisms. This biological fouling is a serious economic problem in industrial water process systems, pulp and paper production processes, cooling water systems, injection wells for oil recovery, cooling towers, porous media (sand and soil), marine environments, and air conditioning systems, and any closed water recirculation system.

[0174] The removal or prevention of biofilm traditionally requires the use of dispersants, surfactants, detergents, enzyme formulations, anti-microbials, biocides, boil-out procedures, and/or corrosive chemicals, e.g., base. Procedures for using these measures are well known in the art. For example, removal of biofilm build-up in a paper machine in the pulp and paper industry traditionally requires a deposit control program including proper housekeeping to keep surfaces free of splashed stock, anti-microbial treatment of fresh water and additives, the use of biocides to reduce microbiological growth on the machine, and scheduled boil-outs to remove the deposits that do form.; wherein the composition is an aqueous, or non-aqueous carrier formulation[0180] The composition comprising one or more polypeptides having lactonohydrolase activity may be a liquid, spray, or powder formulation. A powder carrier is a non-aqueous carrier that is dried. [0180] one or more agents for degrading, removing, or preventing the formation of the biofilm. These agents may include, but are not limited to, dispersants, surfactants, detergents, enzyme formulations, anti-microbials, and biocides. [0181] In a preferred embodiment, the agent is a surfactant. In a more preferred embodiment, the surfactant is sodium dodecyl sulfate, quaternary ammonium compounds, alkyl pyridinium iodides, Tween 80, Tween, 85, Triton X-100, Brij 56, biological surfactants, rhamnolipid, surfactin, visconsin, or sulfonates. [0183] The present invention also relates to such compositions for preventing development of a biofilm. Furthermore, the composition may be a disinfectant composition. [0187] …. the enzyme may be cell-bound, immobilized on a carrier, or used in a free form using methods well known in the art for enzymatic optical resolution.

The US Federal Circuit has recently explicitly stated that in order to make a *prima facie* case of obviousness, the suggestion and motivation to combine said references need not be explicitly stated in the text of the references. Rather, consideration of common knowledge and common sense when combining references is not only permitted *but required*. See DyStar Textilfarben GmbH & Co. Deutschland KG v. C.H. Patrick Co., 80 USPQ2d 1641 (Fed. Cir. 2006) which states:

> ""Suggestion" test for obviousness does not require that suggestion, teaching, or motivation to combine cited prior art references be found in references themselves, or that such suggestion or motivation be explicitly stated; suggestion test is flexible rather than rigid and categorical, recognizing motivation to combine found in knowledge of persons of ordinary skill in art or nature of problem to be solved, as well as in references, and test not only permits, but requires,

consideration of common knowledge and common sense."

Additionally, *KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007), discloses that if a technique has been used to improve one method , and a person of ordinary skill would recognize that it would be used in similar methods in the same way, using the technique is obvious unless its application is beyond that person's skill. *KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007) also discloses that "The combination of familiar element according to known methods is likely to be obvious when it does no more than yield predictable results". It well known in the art to use biocides/detergents, sprays, non-aqueous carriers (Berka) in the formulation of compositions to prevent/reduce/treat bacterial biofilms (Zhang and Berka) in a method of regulating quorum sensing in a bacteria h, therefore one of skill in the art would recognize that there is a need art to solve the problem of reducing biofilm formation on catheters, contact lens and medical devices (Berka) and Zhang et al provide a solution to this problem, by preparing a peptide hydrolase (acylase that cleaves a peptide bond) that serves this need in the art. Thus, it would be obvious to apply a known technique to a known product to be used in a known method that is ready for improvement to yield predictable results.

It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose in order to form a third composition that is to be used for the very same purpose: idea of combining flows logically from their having been individually taught in the prior art" In re Kerkhoven (205 USPQ 1069, CCPA 1980. Zhang et al in view of Berka obviate the instantly claimed invention as now claimed.

Conclusion

17. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to GINNY PORTNER whose telephone number is (571)272-0862. The examiner can normally be reached on flextime, but usually M-F, alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Mondesi can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Robert B Mondesi/
Supervisory Patent Examiner,
Art Unit 1645

/Ginny Portner/
Examiner, Art Unit 1645
July 30, 2010

Aculeacin A acylases purified from *A. utahensis* catalyze the hydrolysis of the amide bond on the palmitoyl side chain of aculeacin A (29). The primary structure of the protein, as well as enzyme activity analysis with different substrates, discussed below, therefore indicates that *qsbA* encodes an AHL-acylase which cleaves the amide linkage between the acyl side chain and the homoserine lactone moiety of AHLs.

[00028] The presumed α and β subunits of QsbA are located at amino acid positions 36-217 and 233-794, respectively, of SEQ ID NO: 2, with a 15 amino acid spacer between them, as determined by alignment with the peptide sequences from *D. radiodurans* strain R1, *A. utahensis* and *P. Aeruginosa*. See Table II.

WO2003/068951

[00031] QsbA and *qsbA* provide new tools for down regulation of AHL-mediated biological activities, such as the expression of virulence genes and biofilm differentiation in pathogenic bacteria, both *in vitro* and *in vivo*. The *qsbA* gene, which

[00041] It has been previously demonstrated that quenching bacterial quorum sensing by inactivation of N-acyl homoserine lactone with AHL-lactonase stops bacterial infection (9, 10). The gene and protein described here, which is likely an AHL-acylase, represent a new and effective tool for inactivation of AHL signals and thus control bacterial infection. Similarly,

the gene and protein described here targets AHL quorum-sensing signals that regulate expression of pathogenic genes of many bacterial pathogens at a threshold concentration. This tool is applicable to all plant, animal or human diseases where the expression of pathogenic genes of bacterial pathogens is activated by AHL signals, such as, for example, plant pathogens *Erw. carotovora*, *Erw. Chrysanthemi*, *Erw. Stewartii*; human pathogens *P. aeruginosa*, *B. cepacia*; and animal pathogens *M. nematophilus*, *P. fluorescens* (1, 3, 6, 12, 17, 19, 22, 23, 24, 26).